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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,493	08/21/2003	Eric Rose	50634-BA	9464

7590 06/07/2006

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 06/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,493	ROSE ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 9 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 9 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicant's election with traverse of the species of Group 18 in the reply filed on August 22, 2005 is acknowledged. Applicants' arguments with respect to the rejoinder of the species of Groups 10 and 21 are convincing, and they have been re-joined and examined with the elected species.

The requirement is still deemed proper and is therefore made FINAL.

It is noted that in the amendment filed May 3, 2006, Applicants canceled from the claims the elected species plus all other species indicated in the previous Office action as being novel and unobvious over the prior art of record. The examiner will continue examination of the remaining Markush claim in accordance with the procedures set forth in MPEP 803.02, i.e. the examiner will examine the remaining claim to the extent necessary to determine its patentability but will not necessarily examine all non-elected species.

2. Claim 9 is deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent applications PCT/US97/08282 and U.S. application serial no. 08/648,561 because the parent applications, under the test of 35 U.S.C. 112, first paragraph, disclose the claimed invention.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by the Liebman abstract (Blood, Vol. 84, No. 10, Suppl. 1, page 66A, Abstract 253). The Liebman abstract teaches an isolated Gla-deficient Factor IX which acts as a Factor IX inhibitor. The Liebman abstract's Gla-deficient Factor IX corresponds to Applicants' carboxylated Christmas factor, because "Factor IX" is a synonym for "Christmas factor", and because the Gla-deficient Factor IX is

partially carboxylated, thus meeting the claim limitation "carboxylated". The Liebman abstract's Gla-deficient factor IX does not undergo a Ca(II)-dependent transition in its tertiary structure, and thus also corresponds to Applicants' Factor IX lacking a calcium-dependent membrane binding function. Note that an intended use limitation, i.e. "pharmaceutical", does not impart patentability to product claims where the product is otherwise anticipated by the prior art.

5. Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by the Miyata et al article (British Journal of Haematology, Vol. 88, pages 156-165) in view of the Rees et al article (EMBO J, Vol. 7, pages 2053-2061). With respect to part (i) of the claim, the Miyata et al article teaches Factor IX Bm Kiryu, isolated and purified and in the form of a buffered saline solution. See page 157, column 1, last paragraph. "Factor IX" is a synonym for "Christmas factor", and Factor IX Bm Kiryu is a "Factor IXa compound" as the phrase is defined in Applicants' specification at page 9, lines 7-19. The Factor IX Kiryu of the Miyata et al article has an intact Ca^{2+} binding site (see page 164, first full paragraph), and therefore inherently will comprise carboxylated glutamic acid residues because the Rees et al article teaches such residues are necessary for Ca^{2+} binding (see the Abstract and page 2053, column 1, first paragraph). The carboxylated glutamic residues that are inherently present in the Factor IX Kiryu of the Miyata et al article thus satisfy the requirement for a "carboxylated" Christmas factor as required by instant claim 9, part (i). With respect to part (iii) of the claim, the Miyata et al article teaches Factor IXa Bm Kiryu in the form of a buffered saline solution. See page 157, column 2, first and third full paragraphs. Factor IXa Kiryu has only 2.5% of the activity of Factor IXa (see, e.g., the Abstract) and thus satisfies Applicants' claim requirement for a "Factor IXa compound". The Factor IX Kiryu has an intact Ca^{2+} binding site (see page 164, first full paragraph), and the activated factor

would have been expected inherently to retain the intact Ca^{2+} binding site because activation is a proteolytic event occurring at sites in Factor IX not involved in Ca^{2+} binding. The Rees et al article teaches that a β-hydroxylated aspartic acid is essential for Ca^{2+} binding to factor IXa (see, e.g., the Abstract). Accordingly, the intact Ca^{2+} binding site present in the Factor IXa Kiryu of the Miyata et al article inherently will comprise a β-hydroxylated aspartic acid as required by instant claim 9, part (iii). Note that an intended use limitation, i.e. "pharmaceutical", does not impart patentability to product claims where the product is otherwise anticipated by the prior art.

6. Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by the Benedict et al article (J. Clin. Invest., Vol. 88, pages 1760-1765). The Benedict et al article teaches an aqueous saline solution comprising bovine Factor IXa inactivated with Glu-Gly-Arg-chloromethylketone. The composition is used as a thrombosis inhibitor. See, e.g., the Abstract; page 1760, column 2, first full paragraph; and Table 1. The inactivated bovine Factor IXa of the Benedict et al article inherently has already been subjected to the post-translational modifications propeptide cleavage, glycosylation, and β-hydroxylation of aspartic acid, because these post-translation modifications occur naturally during the formation of Factor IX and prior to the formation of Factor IXa. The inactivated bovine factor IXa of the Benedict et al article thus corresponds to the Factor IXa compound of section (iii) of Applicants' claim. In view of the similarity in structure and function between the compositions comprising inactivated bovine Factor IXa of the Benedict et al article and Applicants' claimed pharmaceutical compositions, the former are deemed to anticipate the latter. Sufficient evidence of similarity is deemed to be present between the two to shift the burden to Applicants to provide evidence that the claimed invention is unobviously different than that of the Benedict et al article.

7. Applicant's arguments filed May 3, 2006 have been fully considered but they are not persuasive.

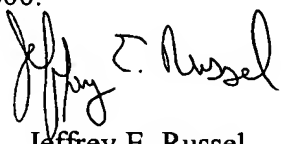
The examiner has interpreted claim 9 as follows: Claim 9 recites a pharmaceutical composition comprising "a factor IXa compound", which the specification at page 8, lines 26-28, defines as being "a compound which inhibits or reduces the conversion of Factor X to Factor Xa by naturally occurring Factor IX". However, claim 9, parts (i) and (iii), recite chemical modifications, i.e. carboxylation, glycosylation, β-hydroxylation, and propeptide cleavage, which are necessary in order for naturally occurring Factor IX to be fully active. See, e.g., the Rees et al article (EMBO J, Vol. 7, page 2053, column 1, first full paragraph of the introduction), and Jallat et al (U.S. Patent No. 5,814,716 at column 1, lines 15-31). Accordingly, while the claim requires the presence of these modifications in the Factor IXa compound, these modifications by themselves can not be responsible for the loss of Factor X conversion activity because, as noted above, these modifications act in favor of Factor X conversion activity. The claim has to be interpreted as permitting modifications to Christmas factor or Factor IXa in addition to those specified in the claims, with the additional modifications resulting in the loss of Factor X conversion activity. In the Miyata et al article (British Journal of Haematology, Vol. 88, pages 156-165), it is the additional Val-313-to-Asp substitution which results in the loss of Factor X conversion activity for Factor IXa Kiryu. In the Benedict et al article (J. Clin. Invest., Vol. 88, pages 1760-1765), it is the inactivation with Glu-Gly-Arg-chloromethylketone which results in the loss of Factor X conversion activity. If Applicants disagree with this interpretation of the claim language, they should explain their interpretation in the response to this Office action, preferably with citations to specific Factor IXa compounds which meet the claim limitations.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1654

JRussel
June 5, 2006